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EXAMINER	
CANELLA, KAREN A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/496,391	Applicant(s) SAN ANTONIO ET AL.	
	Examiner Karen A Canella	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *10-63 and 70-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-9 and 64-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Acknowledgment is made of applicant's election with traverse of Group I, drawn to synthetic peptides comprising the motifs of XBBBXXBX and XBXXBBBX. Applicant has correctly noted and taken into consideration the typographical error of "XBXXXBBBX" which was inadvertently typed to represent XBXXBBBX. The traversal is on the grounds that the restriction is improper as it separates peptides which are not patentably distinct form each other , and therefore a search for Group I peptides would be coextensive for the search for Group II peptides, and the peptide of Group XI. This line of reasoning has been considered but not found persuasive. However, after review and reconsideration of the art with regard to Group I peptides, the inventions of Groups II and XI have been rejoined to Group I for examination at this time. Accordingly, Group IV will be rejoined to Group III, Group VI will be rejoined to Group V, Group VIII will be rejoined to Group VII, and Group X will be rejoined to Group IX based on the rejoinder of peptides having different sequence motif. Further, after review and reconsideration, method claims drawn to the targeting of drugs in a mammal will be examined with methods of modulating tumor cell metastasis (former groups VII and VIII), as well as the collected methods of former groups IX and X. The restriction after rejoined is as follows:

A. (I, II and XI) Claims 1-9 and 64-69, drawn to synthetic peptides, classified in class 530, subclass 300.

B. (III and IV) Claims 16, 25, 34, 43 and 61, drawn to a method of affinity purification using the synthetic peptide of Group I, classified in class 530, subclass 413.

C. (VII, VIII, V in part and VI in part) Claims 12, 21, 30, 39, 48, 57, and claims 14, 23, 32, 41, 50 and 59, in part, drawn to methods for modulating tumor cell metastasis comprising the administration of the peptides of Group I, and methods of targeting drugs in a mammal, classified in class 514, subclass 2. Claims 14, 23, 32, 41, 50 and 59 will be examined with this group to the extend that they read on methods of modulating tumor cell metastasis.

D. (IX, X, V in part, VI in part) Claims 10, 11, 13, 15, 17-20, 22, 24, 26-29, 31, 33, 35-38, 40, 42, 44-47, 49, 51, 52-56, 58, 60, 62, 63, 70-75, and claims 14, 23, 32, 41, 50 and 59, in part, drawn to methods of modulating glycosaminoglycans with anti-coagulant activity, methods of modulating enzymes that act on glycosaminoglycans, methods of blocking tissue uptake and clearance of heparin, methods of promoting wound healing, methods of promoting cell attachment or adhesion and methods for modulating endothelial cell pro-coagulant or anti-coagulant functions, all methods comprising administering the peptide of Group I, and methods of targeting drugs in a mammal, classified in class 514, subclass 2. Claims 14, 23, 32, 41, 50 and 59 will be examined with this group to the extend that they read on methods of modulating glycosaminoglycans with anti-coagulant activity, methods of modulating enzymes that act on glycosaminoglycans, methods of blocking tissue uptake and clearance of heparin, methods of promoting wound healing, methods of promoting cell attachment or adhesion and methods for modulating endothelial cell pro-coagulant or anti-coagulant functions.

Applicant further argues that method claims are not distinct as they represent the all relate to basic methods of using the claimed peptides. Applicant points out that some of the method claims (for instant the method claims of parts C and D above) have the same class subclass designation . Applicant concludes that the search for all the method claims would not present an undue burden on the examiner and therefore should be combined into a single group. Applicant states that the examiner must show by appropriate explanation why said groups are distinct. This has been considered but not found persuasive. As stated above, method claims previously separated by virtue of comprising the different sequence motifs represented by old Group I and II have been rejoined, and method claims drawn to methods of targeting drugs in a mammal will be examined with method claims directed to tumor cell metastasis (new group C) as well as method claims directed to the multiplicity of methods in group D. Further with regard to the inappropriateness of the restriction of inventions which are not distinct, and the examiners lack of commentary about such, it is noted that the methods of Group B differs from the methods of

Groups C and D in the method objectives, method steps and parameters and in the reagents used. The method objective of Group B would be the purification of peptides in vivo. The method objectives of Groups C and D would be treatment of tumor metastasis, and modulation of coagulation and promotion of endothelial cell attachment in a mammal. The reagents used for the method of Group C would not be coextensive with the reagents used in the treatment methods of Groups C and D. Further, the method steps of the invention of Group B would not be the same as the method steps involving the administration of peptides to a mammal in a therapeutic treatment. The method of Group C differs from the method of Group D in method objectives as stated above (method of inhibiting tumor metastasis and methods of modulating coagulation and the promotion of endothelial cell attachment in a mammal). Method steps and reagents used would differ between the two groups because inhibition of tumor cell metastasis would oppose the method of promoting cell attachment in Group D. Further, the patentability requirements would differ between the two groups because the method objectives differ. With regard to the arguments about the burden of the search, it is noted that the literature search which is particularly relevant in this art is not coextensive for Groups B, C and D as the objective of the methods and the steps of the methods differ. Therefore, it would be undue burden on the examiner to search all three method Groups together.

Invention A is related to Inventions B, C and D as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptides of Invention A can be used in any of the methods B through D. In addition, the peptides of Group A can be used in a process to raise an antibody and an anti-idiotypic antibody.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter and because the searches required for the groups are not co-extensive, restriction for examination is deemed proper and adhered to. The restriction requirement is therefore made FINAL.

Claims 1-75 are pending. Claims 10-63 and 70-75, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-9 and 64-69 are examined on the merits.

Claim Objections

Claims 4, 5, 6, 66 and 67 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.. Claims 4, 5, 6, 66 and 67 recite peptide comprises one of the group of D-isomer amino acids. L-isomer amino acids, or a combination of L and D isomer amino acids. L and D isomers refer to the direction of rotation of polarized light (left handed rotation or right handed rotation) which is a result of the three dimensional configuration of the molecule about a tetrahedral carbon atom which serves as a chiral center. It is noted that Glycine is the only amino acid which does not rotate the plane of polarized light as it is lacking a chiral center. The claims require the "B" residue to be either R or K. Both of R or K have chiral centers and rotate the plane of polarized light in either a dextrorotatory or levarotatory fashion. Claims 4, 5, 6, 66 and 67 fail to further limit claims 1-3, 64 and 65 because all of the residues within the peptide of claims 1-3, 64 or 65 must be a L or D amino acid by default in order to meet the limitations of the recited peptide sequences. A peptide comprising only glycine residues would not have D or L amino acids, but would not meets the limitations of claims 1-3, 64 and 65 regarding the specific claimed sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 64-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 68 and 69 recite a "nonconcatameric peptide" with regard to peptide sequence motifs which have an index of n being greater than or equal to one. These repeating units, which have the potential of being two or more, would be a concatamer by nature. It is unclear how the limitation of "nonconcatameric" can be applied to the claimed peptides. For purpose of examination, the claim will be read as any peptide having at least two of the recited sequence motifs separated by at least one of any amino acid.

Claims 68 and 69 recite "Cardin sites". The specification provides no definition for a Cardin site. It appears that the Cardin sites are themselves the sequence motifs of XBBXBX and XBBBXXBX of Cardin and Weintraub (Arteriosclerosis, 1989). The claims describe synthetic peptides wherein Cardin sites are separated by at least one amino acid and wherein the sequence of the synthetic peptide is at least two of the group of (XBBBXXBX)n, (XBXXBBBX)n, (XBBXBX)n or (XBXBBX)n. The metes and bounds of the claim cannot be determined because it is unclear how "Cardin sites" relate to the recited sequence motifs; and it is unclear if the reversed sequences of XBXBBX and XBXXBBBX would be within the scope of a Cardin site, as the specification sets forth no definition of Cardin Site, and the original 1989 publication does not identify the reversed sequences.

Claim 69 recites the limitation of "a single cysteine residues is within three residues of either an N- or C- terminus, either within a Cardin sequence or extended beyond the Cardin sequence. It is noted that the metes and bounds of a "Cardin site" cannot be determined for the reasons set forth above. Further, it is unclear how "Cardin sequence" relates to the "Cardin site" of the second line of the claim, or how a cysteine residue can be within the Cardin sequence or Cardin site, because the claim limits the "X" residues of the sequence motifs to A and G, and the "B" residues to R and K, which excludes the possibility of a "C" within the sequence motifs.

Claims 1-9 and 64-69 recite the limitation of "synthetic" with regard to the claimed peptides. It is unclear if the term "synthetic" includes peptides which are recombinantly produced, or peptides which are produced by means of chemical or enzymatic protein degradation in vitro. Thus, it is unclear if the metes and bounds of the claims exclude only those peptides found in nature, or exclude all peptides with the exception of those chemical synthesized from amino acids, etc.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64 and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al (WO 93/13119) as evidenced by Accession Number AAR42842..

Claim 64 is drawn to a murine serglycin peptide having the sequence of SEQ ID NO:9. Stevens et al disclose a peptide having said sequence in Accession Number AAR42842. It is noted that the claims have been rejected for being vague and indefinite under 112, second paragraph above, because the limitation of "synthetic" was not clear. Stevens et al disclose that the peptide which comprises the claimed SEQ ID NO:9 can be made by recombinant expression in a host cell (for example, page 7, lines 1-4), thus fulfilling the specific embodiment of "synthetic". It is noted that claim 64 also specifies a peptide "having" the amino acid sequence of SEQ ID NO:9. A peptide "having" an amino acid sequence is synonymous with a peptide "comprising" an amino acid sequence, thus when given the broadest reasonable interpretation, the claims are drawn to proteins larger than SEQ ID NO:9. Further, the peptide expressed in a host cell would inherently comprise L-amino acids.

Claims 65 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al (WO 90/00606) as evidenced by Accession Number AAR05247.

Claim 64 is drawn to a murine serglycin peptide having the sequence of SEQ ID NO:10. Stevens et al disclose a peptide having said sequence in Accession Number AAR05247. It is noted that the claims have been rejected for being vague and indefinite under 112, second paragraph above, because the limitation of "synthetic" was not clear. Stevens et al disclose that the peptide which comprises the claimed SEQ ID NO:10 can be made by recombinant expression in a host cell (for example, page 21, second full paragraph), thus fulfilling the specific embodiment of "synthetic". It is noted that claim 64 also specifies a peptide "having" the amino acid sequence of SEQ ID NO:10. A peptide "having" an amino acid sequence is synonymous

with a peptide "comprising" an amino acid sequence, thus when given the broadest reasonable interpretation, the claims are drawn to proteins larger than SEQ ID NO:10. Further, the peptide expressed in a host cell would inherently comprise L-amino acids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over deBoar et al (The Journal of Biological Chemistry, 1992, Vol. 267, pp. 2264-2268) in view of Cardin et al (Arteriosclerosis, 1989, vol. 9, pp. 21-13, reference AD of the IDS submitted March 31, 2003).

Claim 68 is drawn in part to a peptide with a high affinity for glycosaminoglycans and proteoglycans, wherein Cardin sites are separated by at least one of any amino acid and wherein the sequence of said peptide is at least two of the group of (XBBBXXBX)n or (XBBXBX)n, wherein B is arginine or lysine and X is alanine or glycine and n is at least one.

DeBoar et al teach a synthetic peptide comprising residues Lys348 to Arg361 of vitronectin. DeBoar et al teach that these residues include the consensus sequences for

glycosaminoglycan recognition (Figure 5). DeBoar et al teach other peptides which do not include both Cardin sites as indicated by peptides 1 and 3 in figure 5, and that the peptide 2 containing both Cardin sites was the most efficient inhibitor of the binding of the vitronectin thrombin-antithrombin complex to human umbilical vein endothelial cells (page 2267, second column, lines 26-35 under the heading "Discussion"). DeBoar et al teach that peptide inhibition of the binding of the vitroncetin-thrombin-antithrombin complex to the endothelial cells was correlated to the ability of said peptides to directly bind heparin (page 2267, second column, bridging sentence). The Cardin sites in said peptide taught by DeBoar et al are separated by at least one amino acid and the "B" residues are arginine or lysine, however, the X residues are not confined to alanine or glycine. Thus deBoar et al do not teach the instant peptide wherein X is alanine or glycine.

Cardin et al teach the Cardin sites of XBBBXXBX and XBBXBX (abstract). Cardin et al teach that the "B" residues represent a relative probability of basic amino acids and that the "X" residue represents a relative probability of non-basic amino acids in heparin-binding proteins. In the legend for Table 4 (Cardin et al), the "X" residues are broken down statistically to percentage aromatic, acidic and basic. It is noted that adding the percentages of aromatic, acidic and basic for any position gives a percentage far less than 100. Therefore, it is easily deduced that the remainder of the amino acid at the "X" position are neutral or hydrophobic in heparin binding consensus sequences..

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute a "A" or a "G" for any of the positions designated as "X" in the Lys348 to Arg361 peptide as taught by deBoar et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Cardin et al who break down the "X" residue into relative probabilities of related amino acid residues, and the indication that heparin binding consensus sequences have "X" residues that are dominantly neutral or hydrophobic, rather than aromatic, acidic or basic, because these residues represents a small percentage of the "X" residues, and thus, most consensus sequences would be represented by neural or hydrophobic sequences at the "X" positions.

Claims 1, 2, 4, 5, 7, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cardin et al (Arteriosclerosis, 1989, vol. 9, pp. 21-13, reference AD of the IDS submitted March 31, 2003) in view of Wakefield et al (Surgical Research, 1994, Vol. 56, pp. 586-593) and Fromm et al (Archives of Biochemistry and biophysics, 1997, Vol. 343, pp. 92-100, reference AF of the IDS filed March 31, 2003) and Margalit et al (The Journal of Biological chemistry, 1993, Vol. 268, pp. 19228-19231, reference AE of the IDS filed March 31, 2003).

Claim 1 is drawn to a peptide with high affinity for glycosaminoglycans and proteoglycans, wherein the sequence of the amino acids is one of the group of (XBBBXXBX)n or (XBXXBBBX)n, wherein B is arginine or lysine, X is alanine or glycine and n is at least 2. Claim 2 is drawn to a peptide with high affinity for glycosaminoglycans and proteoglycans, wherein the sequence of the amino acids is one of the group of (XBBXBX)n or (XBXBBX)n, wherein B is arginine or lysine, X is alanine or glycine and n is at least 2.. Claims 4 and 5 embody the peptides of claims 1 and 2 wherein the peptide comprises one of the group of D amino acids, L amino acids or a combination of both. Claim 7 is drawn to a peptide with high affinity for glycosaminoglycans and proteoglycans, wherein the sequence of the amino acids is one of the group of (XBBBXXBX)n or (XBXXBBBX)n, wherein B is arginine or lysine, X is any amino acid and n is at least 2. Claim 8 is drawn to a peptide with high affinity for glycosaminoglycans and proteoglycans, wherein the sequence of the amino acids is one of the group of (XBBXBX)n or (XBXBBX)n, wherein B is arginine or lysine, X is any amino acid and n is at least 2.

Cardin et al teach the heparin binding consensus sequences of (XBBXBX) and (XBBBXXBX). Cardin et al teach that "B" is a basic amino acid, therefore fulfilling the specific embodiments of Arg and Lys residues for "B". In the legend for Table 4 (Cardin et al), the "X" residues are broken down statistically to percentage aromatic, acidic and basic. It is noted that adding the percentages of aromatic, acidic and basic for any position gives a percentage far less than 100. Therefore, it is easily deduced that the remainder of the amino acid at the "X" position are neutral or hydrophobic in heparin binding consensus sequences. Thus Cardin et al anticipates the specific embodiment of claims 7 and 8 drawn to any amino acid.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute a "A" or a "G" for any of the positions designated as "X" in the heparin binding consensus sequences as taught by Cardin et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Cardin et al who break down the "X" residue into relative probabilities of related amino acid residues, and the indication that heparin binding consensus sequences have "X" residues that are dominantly neutral or hydrophobic, rather than aromatic, acidic or basic, because these residues represents a small percentage of the "X" residues, and thus, most consensus sequences would be represented by neural or hydrophobic sequences at the "X" positions.

Wakefield et al teach that it is desirable to have an agent which would reverse the effect of low molecular weight heparin (page 590, second column, line 22 to page 591, line 5). Wakefield et al teach that in vivo reversal of heparin depends on the availability of positive charges, but that the greater the net positive charge of the reversing agent, the greater the toxicity of said reversing agent (page 589, second column, bridging sentence to page 590, first column line 3). Wakefield et al teach a variant of protamine which reverses heparin anti-coagulation but retains toxicity (page 591, first column, lines 9-18).

Margalit et al teach that heparin is a negatively charged polymer of regular disaccharides repeat sequences having a high degree of sulfation and that proteins are expected to bind to heparin (page 19228, second column, lines 7-13).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute polymers constructed of repeating units of the Cardin sequence comprising alanine or glycine or any non-basic amino acid at position "X" for the protamine and protamine variants taught by Wakefield et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wakefiled which indicate that undesirable toxicity is correlated with increased negative charge and that the [+18B] protamine variants had a net charge of +18 and was associated with significant toxicity. One of skill in the art could deduce that the binding sequence taught by Cardin et al carried less of a positive charge. However, Wakefield teaches that heparin is a negatively charged polymer. Therefore, in order to reverse the binding effects of heparin to the

thrombin antithrombin complex one of skill in the art would be motivated to have a polymeric agent which would contact heparin across a substantial potion of the molecule. Thus, one of skill in the art would be motivated to use repeating units of the Cardin binding sequence, thus fulfilling the specific embodiments of claims 1 and 2 with respect to a value for "n" which is at least 2. It is noted that the net positive charge for either of the motifs of claim 1 with an index of n=2 would be as low as +8, which would be substantially decreased from the +18 protamine variant used by Wakefield et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
August 11, 2003